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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,526	10/26/2001	Frederick H. Hausheer	X-0211	3276

7590 03/10/2004

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,526	HAUSHEER, FREDERICK H.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

A Request for Continued Examination (RCE) and a Response to the Office Action of November 20, 2003, filed January 26, 2004, are acknowledged and accepted. New claim 16 is presented. Claims 1-16 are now under consideration.

The disclosure is objected to for the following informality: There is no period at the end of claim 16.

Appropriate correction is required.

In the last Office Action the rejection of claims 1, 2, 4-6 and 8 under 35 U.S.C. 102(b) as being anticipated by Plowman et al., Lancet, was maintained. Plowman teaches the parenteral administration of mesna to provide radioprotection at a dose of 400 mg/kg. The rejection of claims 1 and 4 under 35 U.S.C.102(b), as being anticipated by van den Broeke et al., J. Photochem. Photobiol., was further maintained. It was asserted van den Broeke teaches the administration of mesna for UV radiation protection. Previously, there were no responses to either rejection of record.

With respect to the Lancet reference, Applicant presently argues: the claims require that treatment includes the administration of an effective amount of a compound of formula I to a patient who has been exposed to ionizing radiation; the reference is not directed to human patients; the reference fails to disclose an effective amount; and, mesna is not approved for use as a radioprotector.

Applicant's arguments are not found persuasive. The rejection is maintained over claims 1, 2 and 4. The method of claim 1 could be practiced either before or after exposure to ionizing radiation. A laboratory setting, in which mice are utilized, reasonably serves as an appropriate model for humans. The intraperitoneal dose

disclosed in the reference, 400 mg/kg, is encompassed in instant claim 2. Accordingly, Applicant is alleging the effective amounts recited in claims 2 and 6 are toxic amounts at the upper recited limits. According to Facts and Comparisons, the recommended intravenous dose is 0.24 g/m^2. According to Plowman, mesna exhibits radioprotective properties. No standard of practice, or approval for use, was asserted.

Because van den Broeke merely suggests mesna may have UV-radiation protective properties, this rejection of record under 35 U.S.C. 102(b) is withdrawn.

In the last Office Action claims 1-15 were rejected under 35 U.S.C. 103 as being unpatentable over Plowman et al., Lancet . Upon reconsideration this rejection of record is withdrawn.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over van den Broeke et al., J. Photochem. Photobiol.

van den Broeke suggests the administration of mesna for UV radiation protection. See the first line of the abstract where mesna is encompassed among the thiol compounds that may afford protection against damage by radiotherapy. See the last line of the second column on page 279 where application to human subjects is taught. The reference is directed to a laboratory study and does not disclose clinical

applications with respect to optimal modes of administration and dosages. However, one skilled in the radiology art would have been motivated to administer mesna to provide UV-radiation protection in view of the teachings of the reference. Such would have been obvious because van den Broeke demonstrates the ability of thiols, such as mesna, to act as scavengers of reactive radicals and quench molecular oxygen species to afford protection against the damaging effects of radiation. Mesna is well established in the prior art for parenteral administration at recommended doses of 024 g/m^2. It is conventional practice in the pharmaceutical arts, where a compound exhibits efficacy in a particular dosage form, motivation is provided to prepare other dosage forms.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as lacking a clear written description of the invention and of the manner and process of practicing it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the same, and, as not setting forth the best mode contemplated by the inventor to carry out the invention.

The claims are directed to methods of treating a patient for exposure to ionizing radiation and of prophylactically treating a patient about to undergo radiation therapy comprising administering a compound of instant formula I, wherein R_1 is optionally "a sulfur-containing amino acid". The specification discloses no examples wherein an amino acid containing sulfur is utilized. This option finds no support in the specification. There is no showing that Applicant had possession of the claimed invention of therapeutic treatments comprising administering a compound of instant formula I

wherein a sulfur-containing amino acid is utilized. The present level of skill in the radiology art is immature with respect to radioprotection and would reasonably require a more detailed written description directed to the preparation and administration of compounds of instant formula I wherein a sulfur-containing amino acid is present.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to methods of treating a patient for exposure to ionizing radiation and of prophylactically treating a patient about to undergo radiation therapy comprising administering a compound of instant formula I. The specification provides no support specifically directed to treatments wherein an outcome following the administration of such compounds shows any results whatsoever.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to treatment methods for exposure to ionizing radiation and of prophylactically treating a patient about to undergo radiation therapy.

The relative skill of those in the art is generally that of a Ph.D. or M.D. with expertise in the field of radiology.

The broad recitations "treating a patient for exposure to ionizing radiation" and "prophylactically treating a patient about to undergo radiation therapy" are inclusive of many conditions and side effects that presently have no established successful therapies or resolution.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any parameter of ionizing radiation and radiation therapy.

The amount of direction or guidance provided and the presence or absence of working examples

There are no working examples that specifically support the claimed invention.

The quantity of experimentation necessary

Applicant has failed to provide guidance as to which particular compound of instant formula I would be preferred for treatment of the many possible effects of ionizing radiation. The skilled artisan would expect the interaction of a particular compound in the treatment of a particular effect of ionizing radiation to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such understanding nor any criteria for extrapolating beyond the preferred embodiments disclosed in the specification which are solely directed to dosage forms, modes of administration and dosages. Absent reasonable *a priori* expectations of success for using a particular chemotherapeutic compound to treat a particular effect of ionizing radiation, one skilled in the radiology art would have to test extensively many agents to discover which particular effect responds to a particular agent. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis G. Spivack at telephone number 571-272-0585.

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

PHYLLIS SPIVACK
PRIMARY EXAMINER

March 6, 2004